REMARKS

I. Status Summary

Claims 1-99 were pending in the subject U.S. patent application. Claims 1-99 as filed were subjected to a Restriction/Election Requirement. In response to the Restriction/Election Requirement, applicants elected the claims of Group 1, claims 1-19; species election, cell; for prosecution. As a result of the elections, claims 1-3 and 7-19 are pending and have been examined.

The specification has been objected to upon the following contentions. First, Figure 1A discloses sequences that are not accompanied by the required reference to the relevant sequence identifiers. Second, the Paper Copy and the CRF of the Sequence Listing do not match. Third, the specification contains an embedded hyperlink. And last, the title is not descriptive.

Claim 8 has been objected to based on the presence of the phrase "is comprises a polypeptide".

Claims 1-3 and 7-19 have been rejected on two bases under 35 U.S.C. § 112, first paragraph, upon the contentions set forth on pages 4-8 of the Official Action.

Claims 1-3 and 7-19 have also been rejected on several bases under 35 U.S.C. § 112, second paragraph, upon the contentions set for on page 9 of the Official Action.

Claims 1, 7-11, and 15-17 have been amended. Support for the amendments can be found throughout the specification as filed. No new matter has been added by the amendments to the claims or the addition of the new claims. Reconsideration of the application as amended and based on the arguments set forth herein below is respectfully requested.

II. Responses to the Objections to the Specification

The specification has been objected to upon the following four contentions. First, Figure 1A discloses sequences that are not accompanied by the required reference to the relevant sequence identifiers. Second, the Paper Copy and the CRF of the Sequence Listing do not match. Third, the specification contains an embedded hyperlink. And last, the title is not descriptive. Applicants submit the following to address these objections.

With regard to the first objection, applicants have amended the first paragraph of the section of the specification entitled "Brief Description of the Drawings" to reflect that the sequences disclosed in Figure 1A correspond to the amino acid sequences of a rat KCR1 polypeptide and a human KCR1 polypeptide as set forth in SEQ ID NOs: 9 and 2, respectively.

With regard to the differences between the paper and CRF copies of the Sequence Listing, applicants hereby submit a Substitute Sequence Listing that corrects the discrepancies as well as adds SEQ ID NOs: 8 and 9, which correspond to a nucleic acid and deduced amino acid sequence of a rat KCR1 cDNA. The inclusion of these sequences in the Substitute Sequence Listing is necessitated by the amendment to the specification to reference the sequences disclosed in Figure 1A. Support for the addition of these sequences to the Substitute Sequence Listing can be found in Figure 1A and in the specification as filed, including particularly at page 95, line 13, which discloses that the rat nucleic acid and deduced amino acid sequences correspond to GenBank® Accession No. U78090. The sequences disclosed at this Accession No. are exactly the sequences added as SEQ ID NOs: 8 and 9. Thus, no new matter has been added by the submission of the Substitute Sequence Listing.

The third objection to the specification concerns the presence of an embedded hyperlink. Applicants have amended the specification at pages 23, 42, and 106 to remove the "http://www." from each URL. Applicants respectfully submit that these changes address the instant rejection.

And finally, the specification has been objected to upon the contention that the title is not descriptive. Applicants have amended the specification, replacing the title with a title substantially identical to that suggested by Examiner Bunner. Applicants would like to express their thanks to Examiner Bunner for her suggestion.

As a result of the amendments to the specification outlined hereinabove, applicants respectfully submit that the objections to the specification have been addressed. Applicants respectfully request that the objections to the specification be withdrawn.

III. Responses to the Objections to the Claims

Claim 8 has been objected to on the basis that the claim recites "is comprises a polypeptide". Claim 8 has been amended to remove the word "is" from this claim, which applicants believe addresses the instant objection. Applicants respectfully request that the objection to claim 8 be withdrawn.

IV. Responses to the Rejections under 35 U.S.C. § 112, First Paragraph

Claims 1-3 and 7-19 have been rejected under 35 U.S.C. § 112, first paragraph, upon the contentions that the specification as filed fails to comply with the enablement and written description requirements set forth therein. The bases for these rejections are presented on pages 4-8 of the Official Action. After careful consideration of these rejections and the Patent Office's bases therefor, applicants respectfully traverse the rejections and submit the following remarks.

A. The Enablement Rejection

The Patent Office's contentions regarding the teachings of the specification, including the embodiments conceded by the Patent Office to be enabled, are outlined on pages 4-6 of the Official Action. Summarily, the Patent Office concedes that the specification enables a method of identifying a compound that increases or decreases the transmission of potassium ions through a HERG potassium channel, comprising: (a) culturing a cell comprising the HERG potassium channel of SEQ ID NO: 3 and a KCR1 polypeptide encoded by the nucleic acid sequence of SEQ ID NO: 1; (b) contacting the cell with a test compound; (c) measuring the transmission of potassium ions through the HERG channel in the presence of the test compound; and (d) comparing the potassium ion transmission through the HERG channel in the presence of the test compound with that in the absence of the test compound. However, the Patent Office asserts that the specification does not fully enable the method recited in claim 1 as filed. In particular, the Patent Office asserts that the specification does not teach (a) screening for substances capable of modulating potassium channels other than HERG in conjunction with a human KCR1 polypeptide encoded by SEQ ID NO: 1; or (b) that all potassium channels are capable of interacting with KCR1. Further, the Patent Office contends that

undue experimentation would be necessary to screen all possible potassium channels with all possible compounds for all possible biological activities.

Applicants initially respectfully submit that as a matter of Patent Office practice, the burden rests upon the Patent Office to establish a prima facie case of a failure to comply with 35 U.S.C. § 112, first paragraph, with respect to the invention described and claimed in applicants' presumptively enabling patent application. See In re Marzocchi, 58 C.C.P.A. 1069, 439 F.2d 220, 169 U.S.P.Q. 367 (C.C.P.A. 1971).

The Patent Office contends that the specification of the present U.S. patent application does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with the claims. However, no specific scientific or other factual basis in support of this contention has been presented in the Official Action. Indeed, the Patent Office has cited no patents, no journal articles, and no other references in support of its position, other than to assert that potassium channels make up a large class of proteins.

Applicants submit that the Patent Office has not met its burden, as is required under In re Marzocci. Rather, the Patent Office has offered only a series of conclusory statements, contending:

> due to the large quantity of experimentation necessary to screen all possible potassium channels with all possible compounds for all possible biological activities, the lack of direction/guidance presented in the specification regarding the same, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the structural and functional diversity of potassium channels, and the breadth of the claims which fail to recite any limitation as to the potassium channel and biological activity to be examined in the assay, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Official Action at page 6.

Applicants respectfully submit that a prima facie case of a lack of enablement under 35 U.S.C. § 112, first paragraph, has not been made. Indeed, 35 U.S.C. § 112, first paragraph, requires no more than a disclosure sufficient to enable one skilled in the art to carry out the invention commensurate with the scope of the claims, and this requirement has clearly been met. Accordingly, claims 1-3 and 7-19 are believed to be

in compliance with 35 U.S.C. §112, first paragraph. Withdrawal of this rejection of claims 1-3 and 7-19 is respectfully requested.

However, assuming arguendo that the Patent Office has made out a prima facie case of a failure to comply with 35 U.S.C. §112, first paragraph, applicants respectfully submit the following. The Patent Office's primary contention in support of the rejection under 35 U.S.C. §112, first paragraph, appears to be that undue experimentation would be required to use the entire scope of the claimed invention. Official Action at page 6. It also appears that it is the Patent Office's position that 35 U.S.C. §112, first paragraph, requires the presentation of working examples with respect to all different classes of potassium channels. Applicants respectfully submit, however, that an inappropriate standard for measuring enablement under 35 U.S.C. §112, first paragraph, has been adopted. The appropriate standard is that the claimed invention must be enabled so that a person skilled in the art can make and use the invention from the disclosures of the specification, coupled with information known in the art, without "undue experimentation". In re Wands, 8 U.S.P.Q. 2d 1400, 1404 (Fed. Cir. 1988).

In the Official Action the Patent Office contends that "undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope." Official Action at page 6. Indeed, while it might require considerable experimentation to practice the instant invention, the quantity of experimentation to be performed by one skilled in the art is only one factor involved in determining whether "undue experimentation" is required to make and use the invention. "An extended period of experimentation may not be undue if the skilled artisan is given sufficient direction or guidance." In re Colianni, 195 U.S.P.Q. 150, 153 (C.C.P.A. 1977). "The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which experimentation should proceed." In re Wands, 8 U.S.P.Q. 2d at 1404 (citing In re Angstadt, 190 U.S.P.Q. 214, 218 (C.C.P.A. 1976)). Time and expense are merely factors in this consideration and are not the controlling factors. U.S. v. Telectonics, Inc., 8 U.S.P.Q. 2d 1217, 1223 (Fed. Cir. 1988), cert. denied, 490 U.S. 1046 (1989). It is further noted

that the level of skill in this art is high. As noted in the In re Wands decision, this factor must also be considered in evaluating compliance with 35 U.S.C. §112, first paragraph.

While the presence or absence of working examples is one consideration in the overall evaluation of enablement, working examples are not required under 35 U.S.C. §112, first paragraph, to comply with the enablement standard presented therein. Indeed, the Manual of Patent Examining Procedure (hereinafter the "MPEP") states that the specification need not contain an example if the invention is otherwise disclosed in such a manner that one skilled in the art will be able to practice it without an undue amount of experimentation. MPEP §2164.02. The MPEP also states that a lack of working examples or lack of evidence that the claimed invention works as described should never be the sole reason for rejecting the claimed invention on the grounds of lack of enablement. Id. (emphasis added).

Initially, applicants respectfully traverse the assertion that the specification is absent working examples applicable to the method of claim 1. Applicants respectfully submit that the specification as filed supplies ample working examples for a structure comprising a potassium channel, wherein the potassium channel comprises a potassium channel polypeptide and KCR1, contacting the potassium channel with a test compound, and determining potassium transmission by the potassium channel in the presence or absence of the test compound. Since the nature of the specific potassium channel polypeptide and the test compound employed do not impact the assay, applicants respectfully submit that the disclosed techniques can be used to test any test compound on any structure comprising a KCR1 polypeptide and any other potassium channel polypeptide.

Applicants have amended claim 1 to recite that the biological activity of the potassium channel to be assayed is potassium transmission. Support for this amendment can be found throughout the specification as filed, including particularly at page 14, lines 27-30, wherein transmission of potassium ions through a HERG channel is listed as a representative, non-limiting, example of a "biological activity" of the presently disclosed subject matter. Thus, the claims recite assaying a "structure comprising a potassium channel, wherein the potassium channel comprises a potassium channel polypeptide and a potassium channel regulator 1 (KCR1)

polypeptide" for transmission of potassium ions in the presence and absence of the test compound. Applicants further submit that applicable assays are provided, namely the patch clamp or voltage clamp protocols that are used to measure potassium currents, and further that these and other appropriate assays are well known to those of skill in the art. Thus, applicants respectfully submit that the specification clearly teaches that patch clamp or voltage clamp assays can be used to test the ability of test compounds to modulate potassium transmission in structures (such as cells) that contain any potassium channel polypeptide and KCR1.

Furthermore, the Patent Office concedes that the specification teaches that CHO-K1 cells can be transiently transfected with plasmids encoding potassium channel polypeptides and that voltage clamp protocols are used to measure potassium currents. Applicants respectfully submit that while the specification teaches that the cells were transfected with HERG, KCR1, and MiRP1, any other potassium channel polypeptide could be used in place of HERG. Furthermore, the amount of experimentation necessary to determine whether a test compound modulated the activity of a potassium channel comprising this other potassium channel polypeptide would be no greater than that required to test the HERG channel exemplified in the working examples.

Additionally, the Patent Office appears to be considering it undue experimentation to screen all possible potassium channels with all possible compounds. Applicants respectfully submit that this is also an improper basis for rejecting claim 1 and dependent claims thereof under 35 U.S.C. § 112, first paragraph. Applicants submit that the claims do not require that all possible channels or compounds be screened. Rather, the method recites that a structure comprising a potassium channel polypeptide and KCR1 is provided, and that the structure is contacted with the test compound. Applicants have already addressed the ability of the skilled artisan to produce the required structure using any potassium channel polypeptide and KCR1. Furthermore, any test compound can be assayed as taught in the specification. Thus, while it might require considerable effort to screen all possible potassium channels with all possible compounds, applicants respectfully submit that this is not required by the claims. Furthermore, even assuming arguendo that the method of claim 1 did seek to identify all possible compounds that modulate all possible potassium channels, the

experimentation required would not be undue. Stated another way, applicants respectfully submit that the amount of experimentation cannot be considered undue just because the number of potential candidates to be tested is large, particularly when, as here, the method steps themselves are adequately disclosed and enabled.

And finally, the Patent Office asserts that "the specification also does not disclose that all potassium channels are capable of interacting with the KCR1 polypeptide, as required by the claims". Official Action at page 6. Applicants respectfully traverse the assertion that the claims require that the potassium channel polypeptide and the KCR1 polypeptide interact. Claim 1 recites the following:

1. A method of identifying a compound that modulates potassium transmission by a potassium channel, comprising:

(a) providing a structure comprising a potassium channel, wherein the structure comprises a potassium channel polypeptide and a potassium channel regulator 1 (KCR1) polypeptide;

(b) contacting the test compound with the structure;

(c) determining potassium transmission by the potassium channel in the presence of the test compound; and

(d) comparing the potassium transmission by the potassium channel in the presence of the test compound to potassium transmission by the potassium channel in an absence of the test compound, wherein a difference between potassium transmission by the potassium channel in the absence of the test compound and potassium transmission by the potassium channel in the presence of test compound indicates modulation of potassium transmission by the potassium channel.

As can be seen, the plain language of the claim does not require that the potassium channel polypeptide and the KCR1 interact. It only requires that the structure comprising the potassium channel comprise both a potassium channel polypeptide and a KCR1 polypeptide. Thus, whether or not a given potassium channel polypeptide interacts with KCR1 is not relevant to the instant claims. Furthermore, since claim 1, subsection (a), requires that a structure comprising a potassium channel be provided,

the claim only requires that the potassium channel polypeptide and a KCR1 polypeptide be present in the structure (for example, a cell): it does not require that they interact.

Summarily, applicants respectfully submit that the Patent Office appears to have adopted an improper standard for addressing the enablement of the pending claims. Furthermore, applicants respectfully submit that under viewed under the appropriate standard, the methods recited in independent claim 1 and dependent claims 2-3 and 7-19 are adequately enabled. As a result, applicants respectfully request that the instant rejection of claims 1-3 and 7-19 be withdrawn, and that the claims be allowed at this time.

B. The Written Description Rejection

Claims 1-3 and 7-19 have also been rejected under 35 U.S.C. § 112, first paragraph, upon the contention that the claims contain subject matter that was not described in the specification is such a way as to reasonably convey to one of ordinary skill in the relevant art that the inventors had possession of the claimed invention at the time the application was filed. According to the Patent Office, the specification does not teach any specific potassium channels to be utilized in the disclosed assay other than the HERG potassium channel as set forth in SEQ ID NO: 3. Citing case law, the Patent Office appears to be asserting that only for those potassium channels for which the specification explicitly discloses the nucleic acid and/or amino acid sequences is the written description satisfied. Applicants have carefully reviewed the instant rejection and the Patent Office's bases therefor, and respectfully submit that the Patent Office has adopted an improper standard in applying the holdings of the cited cases to the current disclosure.

Applicants initially note that as a matter of Patent Office practice, the burden rests upon the Patent Office to establish a prima facie case of a failure to comply with 35 U.S.C. § 112, first paragraph, with respect to the invention described and claimed in applicants' patent application. See Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1, "Written Description" Requirement (hereinafter "The Guidelines"), 66 Fed. Reg. at 1105. This includes "the initial burden, after a thorough reading and evaluation of the content of the application, of presenting

evidence or reasons why a person skilled in the art would not recognize in an applicant's disclosure a description of the invention defined by the claims". Id. Additionally, The Guidelines state that there is a "strong presumption that an adequate written description of the claimed invention is present in the specification as filed". Id., citing In re Wertheim, 541 F.2d 257, 262 (CCPA 1976). Furthermore, the Patent Office must establish "by a preponderance of the evidence why a person skilled in the art would not recognize in an applicant's disclosure a description of the invention defined in the claims". Id. at 1107, citing Wertheim, at page 263.

The Patent Office contends that the specification of the present U.S. patent application does not show that applicants were in possession of the claimed invention. However, no specific scientific or other factual basis in support of this contention has been presented in the Official Action. Rather, the Patent Office has offered only a series of conclusory statements, contending generally that the specification of the present patent application does not adequately describe to one of skill in the art "the potassium channels of the encompassed methods". Official Action at page 8. According to The Guidelines, "a general allegation of 'unpredictability in the art' is not a sufficient reason to support a rejection for lack of adequate written description". The Guidelines at page 1107. Indeed, 35 U.S.C. §112, first paragraph, requires no more than a disclosure sufficient to convey to one of ordinary skill in the art that applicants were in possession of the invention commensurate with the scope of the claims (see The Guidelines at page 1105, citing Wang Labs. v. Toshiba Corp., 993 F.2d 858, 865 (Fed. Cir. 1993)), and this requirement has clearly been met. As a result, applicants respectfully submit that a prima facie case under 35 U.S.C. §112, first paragraph, has not been made out. Accordingly, 1-3 and 7-19 are believed to be in compliance with 35 U.S.C. §112, first paragraph. Withdrawal of this rejection of these claims is respectfully requested.

However, assuming arguendo that the Patent Office has made a prima facie case of a failure to comply with 35 U.S.C. §112, first paragraph, applicants respectfully submit the following.

The Patent Office's primary contention in support of the rejection under 35 U.S.C. §112, first paragraph, appears to be that the specification does not provide adequate

written description for the broad class of all potassium channels. The Patent Office appears to contend that the holdings of Fiers v. Revel, Amgen v. Chugai, and Fiddes v. Baird compel the production of the exact amino acid sequences for all potassium channel polypeptides that can be used in the claimed method. Applicants respectfully note that, contrary to the Patent Office's assertions, this line of cases is inapplicable to the current rejection, and that the holdings in these cases involved issues and facts that are not clearly applicable to the claimed method.

In Amgen v. Chugai, the Court of Appeals for the Federal Circuit (hereinafter the "C.A.F.C.") held that "when an inventor is unable to envision the detailed constitution of a gene so as to distinguish it from other materials, as well as a method for obtaining it, conception has not been achieved until reduction to practice has occurred, i.e. until after the gene has been isolated" (emphasis added). Amgen v. Chugai involved claims to the human erythropoietin nucleotide sequence based upon the peptide sequence of the human erythropoietin protein. Due to the redundancy of the genetic code, the C.A.F.C. held that possession of the polypeptide sequence did not result in possession of the nucleotide sequence. In Fiers v. Revel, the C.A.F.C. held that conception of a DNA sequence coding for a particular protein does not occur upon conception solely of a method of obtaining it. Relying on Amgen v. Chugai, the C.A.F.C. reiterated that conception of a DNA sequence of a product having a particular biological activity or function is not complete until one can define the DNA sequence by other than the particular biological activity or function of the encoded gene. And finally, in Fiddes v. Baird, the Board of Patent Appeals and Interferences held that Fiddes' claims to a human gene for basic fibroblast growth factor were separately patentable over party Baird's claims reciting a sequence encoding "mammalian" basic fibroblast growth factor.

These cases are inapplicable to the current invention because their holdings are based upon the unpredictability of the art of cloning genes and cDNAs. The cited cases involve situations where the applicants tried to show conception of a specific human cDNA sequence based upon general methods for cloning a cDNA sequence in conjunction with knowledge of, 1) a protein sequence (Amgen and/or Fiddes); or 2) a functional activity (Fiers). In each case, the C.A.F.C. pointed out that the specific nucleotide sequence could not be envisioned until a reduction to practice had occurred

because a specific DNA sequence cannot be predicted from a protein sequence, a functional description, or a homologous gene from another species.

This is not the situation presented by the present application. For example, applicants respectfully submit that they are not claiming the potassium channel polypeptides per se in claim 1, and thus a specific enumeration of amino acid sequences of all potassium channel polypeptides is not required. The method, rather, is one that can be applied to any potassium channel polypeptide, and further that the method does not change irrespective of the potassium channel polypeptide. By way of analogy, a method claim reciting the use of a personal computer would not require that all appropriate personal computers be specifically recited in the specification.

Furthermore, applicants submit that the written description requirement does not require an applicant to disclose that which is known to those of skill in the art. Accordingly, applicants respectfully submit that the written description requirement does not demand, for example, that applicants disclose the sequences of all potassium channel polypeptides that were known as of the date of filing of the instant application, as that information is within the knowledge of one of ordinary skill in the art. As such, at a minimum, applicants are in possession of every potassium channel the sequence for which was publicly available as of the filing date of the instant application.

The Patent Office also asserts that Vas-Cath Inc. v. Mahurkar "clearly states that 'applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." Official Action at page 8. Applicants respectfully submit, however, that the Patent Office is also overstating the holding of Vas-Cath. In Vas-Cath, the Federal Circuit held that written description is a question of fact, which depends on the nature of the invention and the amount of knowledge imparted to those skilled in the art by the disclosure. Id. at 1562. Based on this principle, the court also held that a determination of written description as required by 35 U.S.C. § 112, first paragraph, must involve a decision on its own facts and that the precedential value of cases in this area is extremely limited. Id. at 1562 (citing In re Driscoll, 562 F.2d 1245, 1250 (CCPA 1977)) (emphasis added). Additionally, The Guidelines also set forth that "[c]ompliance with the written description

is a question of fact which must be resolved on a case-by-case basis." 66 Fed. Reg. at 1104-1105 (citing Vas-Cath).

Applicants respectfully submit that the Patent Office has not undertaken such a case-by-case analysis and that the Patent Office's mere reference to the above-cited cases cannot be simply extrapolated to a finding of lack of written description of the presently pending claims. Based on foregoing arguments, applicants respectfully submit that the rejection of claims 1-3 and 7-19 is not supported by the necessary showing on the part of the Patent Office. Applicants further respectfully submit that the Patent Office has not presented a prima facie case of lack of compliance with the written description requirement of 35 U.S.C. § 112, first paragraph.

Accordingly, claims 1-3 and 7-19 are believed to comply with the written description requirement of 35 U.S.C. § 112, first paragraph. Withdrawal of the rejection of pending claims 1-3 and 7-19 under 35 U.S.C. §112, first paragraph, is therefore respectfully requested. Allowance of claims 1-3 and 7-19 is also respectfully requested.

V. Responses to the Rejections under 35 U.S.C. § 112, Second Paragraph

Claims 1-3 and 7-19 have been rejected under 35 U.S.C. § 112, second paragraph, on several bases. After careful consideration of these rejections and the Patent Office's bases therefor, applicants respectfully traverse the rejections and submit the following remarks.

A. Abbreviations of HERG, KCR1, and MiRP1

Claims 1-3 and 7-19 have been rejected under this section on the basis of the presence of abbreviations for HERG, KCR1, and MiRP1 in some of the claims. Applicants have amended the claims to recite the unabbreviated name for each gene and/or gene product as follows: HERG refers to a human ether-a-go-go-related gene and gene product; KCR1 refers to a potassium channel regulator 1 gene and gene product, and MiRP1 refers to a minK-related peptide-1 gene and gene product. Applicants respectfully submit that the amendments to the relevant claims have addressed the rejections on this basis, and respectfully request the withdrawal of the rejection.

B. "Modulates a Biological Activity"

Claims 1-3 and 7-19 have been rejected under this section upon the contention that the phrase "modulates a biological activity" is a relative phrase that renders the claims indefinite. According to the Patent Office, the phrase is not defined by the claim and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. After careful consideration of the rejection and the Patent Office's bases therefor, applicants respectfully traverse the rejection and submit the following remarks.

With regard to the term "modulates", the Patent Office asserts that it is not clear what limitations the term encompasses. As used in claim 1, the independent claim from which claims 2-3 and 7-19 depend directly or indirectly, the term "modulates" is used to refer to causing a change (for example, a change in a biological activity) that results from the presence or absence of the entity in question (for example, a compound). This particular definition can be discerned from the specification, including, for example, at page 63, lines 20-21, where "transcriptionally modulat[ing] the expression of a gene" is defined as "to change the rate of transcription of such gene". As such, the term "modulates" is synonymous with "changes", "alters", "regulates", etc., and can encompass both positive and negative changes in a biological activity.

As used in the specification as filed, "the term 'modulate' means an increase, decrease, or other alteration of any, or all, chemical and biological activities or properties of a HERG polypeptide and/or KCR1 polypeptide. The term 'modulation' as used herein refers to both upregulation (i.e., activation or stimulation) and downregulation (i.e. inhibition or suppression) of a response". See Specification at page 15, lines 13-17. Thus, in accordance with this definition of "modulate", the phrase "modulates a biological activity of a potassium channel" refers to "causing a change" (for example, inhibiting or stimulating) in a biological activity of a potassium channel. Accordingly, applicants respectfully submit that the phrase "modulates a biological activity" is clearly defined in the instant application when viewed in the context of the specification. However, in an effort to expedite prosecution of the pending claims, applicants have amended claim 1 to recite a method of identifying a compound that modulates potassium transmission by a potassium channel.

As a result of the amendment to claim 1 and the remarks presented hereinabove, applicants respectfully submit that the rejection of claims 1-3 and 7-19 related to the use of the term "modulates a biological activity" has been addressed.

C. "Potassium Channel Polypeptide"

According to the Patent Office, claims 1 and 15 recite the limitation "potassium channel polypeptide" without antecedent basis. The Patent Office has suggested that the rejection could be addressed by amending claims 1 and 15 to recite "potassium channel".

In view of the Patent Office's suggestion, applicants have amended claim 1 to recite the following: a method of identifying a compound that modulates potassium transmission by a potassium channel, comprising: (a) providing a structure comprising a potassium channel, wherein the structure comprises a potassium channel polypeptide and a potassium channel regulator 1 (KCR1) polypeptide; (b) contacting the test compound with the structure; (c) determining potassium transmission by the potassium channel in the presence of the test compound; and (d) comparing potassium transmission by the potassium channel in the presence of the test compound to potassium transmission by the potassium channel in an absence of the test compound, wherein a difference between potassium transmission by the potassium channel in the absence of the test compound and potassium transmission by the potassium channel in the presence of test compound indicates modulation of potassium transmission by the potassium channel.

Similarly, applicants have amended claim 15 to recite the following: the method of claim 1, wherein potassium transmission by the potassium channel in the presence of a test compound is determined in the presence of a minK-related peptide-1 (MiRP1) polypeptide.

Applicants respectfully submit that the amended claims and remarks presented herein address the rejections of claims 1-3 and 7-19 under 35 U.S.C. §112, second paragraph, and that the claims are in condition for allowance. Applicants respectfully solicit a Notice of Allowance to that effect.

CONCLUSIONS

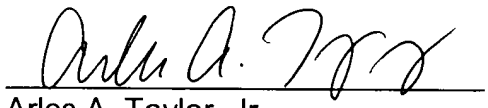
As a result of the amendments to the specification and claims and the remarks presented hereinabove, applicants respectfully submit that claims 1-3 and 7-19 are in condition for allowance. Applicants earnestly solicit a Notice of Allowance to that effect.

If any minor issues should remain outstanding after the Examiner has had an opportunity to study the Amendment and Remarks, it is respectfully requested that the Examiner telephone the undersigned attorney so that all such matters may be resolved and the application placed in condition for allowance without the necessity for another Action and/or Amendment.

DEPOSIT ACCOUNT

The Commissioner is hereby authorized to charge any fees associated with the filing of this correspondence to Deposit Account Number **50-0426**.

Respectfully submitted,
JENKINS, WILSON & TAYLOR, P.A.

Date: 04/07/2004 By: 
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